

08/765,026

attachment to  
Paper #6

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\* W E L C O M E T O T H E \*  
\* U. S. P A T E N T T E X T F I L E \*  
\* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \* \*

=> s adenovir? and superoxide  
2357 ADENOVIR?  
2027 SUPEROXIDE  
L1 113 ADENOVIR? AND SUPEROXIDE  
  
=> s l1 and dismutase  
1056 DISMUTASE  
L2 95 L1 AND DISMUTASE  
  
=> s adenoviral vector? and superoxide dismutase  
141 ADENOVIRAL  
62137 VECTOR?  
65 ADENOVIRAL VECTOR?  
(ADENOVIRAL (W) VECTOR?)  
2027 SUPEROXIDE  
1056 DISMUTASE  
1032 SUPEROXIDE DISMUTASE  
(SUPEROXIDE (W) DISMUTASE)  
L3 6 ADENOVIRAL VECTOR? AND SUPEROXIDE DISMUTASE

=> d 13,1-6,cit,ab

1. 5,670,488, Sep. 23, 1997, Adenovirus vector for gene therapy; Richard J. Gregory, et al., 514/44; 424/93.2; 435/320.1; 935/62 :IMAGE AVAILABLE:

US PAT NO: 5,670,488 :IMAGE AVAILABLE: L3: 1 of 6

ABSTRACT:

Gene Therapy vectors, which are especially useful for cystic fibrosis, and methods for using the vectors are disclosed.

2. 5,641,662, Jun. 24, 1997, Transfection of lung via aerosolized transgene delivery; Robert James Debs, et al., 435/172.1; 128/200.14, 200.24; 424/450; 435/172.3, 320.1; 436/71; 514/44; 536/24.1 :IMAGE AVAILABLE:

US PAT NO: 5,641,662 :IMAGE AVAILABLE: L3: 2 of 6

ABSTRACT:

Methods and compositions for producing a mammal capable of expressing an exogenously supplied gene in cells of the airway are disclosed. Lipid carrier-nucleic acid complexes are prepared then delivered via aerosol to the lung airway. The invention provides a direct method for transforming pulmonary cells as a means for treating disorders of the lung as for providing a means for delivering substances systematically following expression in the lung.

3. 5,599,712, Feb. 4, 1997, Protection from ionizing irradiation or chemotherapeutic drug damage by in vivo gene therapy; Joel S. Greenberger, 435/267; 424/93.2, 93.21; 435/320.1; 514/44 :IMAGE

AVAILABLE:

US PAT NO: 5,571,797 :IMAGE AVAILABLE:

3 of 6

ABSTRACT:

A method of protecting a subject against an agent that elicits production of toxic free radicals, superoxide anions, or heavy metal cations in the subject consisting of the in vivo administration to the subject of a polynucleotide encoding a protein that is transiently expressed in said subject. The transiently expressed protein is capable of neutralizing or eliminating the toxic free radicals, superoxide anions or heavy metal cations that are elicited by the agent. This method is particularly useful in protecting cancer patients against the damaging effects of ionizing radiation and chemotherapeutic drugs.

4. 5,571,797, Nov. 5, 1996, Method of inducing gene expression by ionizing radiation; Tsuneya Ohno, et al., 514/44; 424/1.11, 1.49, 1.61, 1.65, 1.69, 93.2, 93.21, 450; 435/69.1, 69.5, 172.3, 320.1; 536/24.1; 935/6, 34, 59, 62 :IMAGE AVAILABLE:

US PAT NO: 5,571,797 :IMAGE AVAILABLE:

L3: 4 of 6

ABSTRACT:

The present invention provides a method for delivering ionizing radiation to specific tissues, resulting in the activation of a DNA molecule comprising a radiation responsive enhancer-promoter operatively linked to an encoding region that encodes at least one polypeptide. The radiation source may be will generally be in the form of a radionuclide, capable of gamma or beta emissions. Processes for regulating polypeptide expression and inhibiting tumor growth using such DNA molecules are also provided.

5. 5,552,309, Sep. 3, 1996, Use of polyols for improving the introduction of genetic material into cells; Keith L. March, 435/172.3; 424/93.1, 93.2, 426; 435/235.1, 320.1; 514/44; 935/57 :IMAGE AVAILABLE:

US PAT NO: 5,552,309 :IMAGE AVAILABLE:

L3: 5 of 6

ABSTRACT:

A process for introducing an expression vehicle (e.g., plasmids, retroviral vectors, **adenoviral vectors**) into cells, which comprises contacting the cells with the expression vehicle and a polyol. The polyol may be a polyoxalkylene block copolymer, such as a polyoxypropylene-polyoxyethylene block copolymer. The use of the polyol provides for greater efficiency of transduction of the expression vehicle.

6. 5,496,731, Mar. 5, 1996, Broad-spectrum tumor suppressor genes, gene products and methods for tumor suppressor gene therapy; Hong-Ji Xu, et al., 435/320.1; 514/44; 536/23.5 :IMAGE AVAILABLE:

US PAT NO: 5,496,731 :IMAGE AVAILABLE:

L3: 6 of 6

ABSTRACT:

The present invention relates to a broad-spectrum tumor suppressor gene and the protein expressed by that gene in appropriate host cells. The protein is a second in-frame AUG codon-initiated retinoblastoma protein of about 94 kD relative molecular mass. The present invention also relates to methods of treating a mammal having a disease or disorder characterized by abnormal cellular proliferation, such as a tumor or cancer and methods of treating abnormally proliferating cells, such as tumor or cancer cells. Treatment is accomplished by inserting a host cell compatible p94.sup.RB expression vector or an effective amount of p94.sup.RB protein into a cell or cells in need of treatment.

=> d kwic,1

DRAWING DESC:

DRWD (22)

FIGS. 17A and 17B show the plasmid construction for a second generation **adenoviral vector** (Ad2E4ORF6).

DETDESC:

DETD (27)

**Second Generation Adenoviral Vectors**

DETDESC:

DETD (28)

**Adenoviral vectors** currently in use retain most (.gtoreq.80%) of the parental viral genetic material leaving their safety untested and in doubt. Second-generation. . .

DETDESC:

DETD (32)

In . . . deliver CFTR in conjunction with other genes such as anti proteases (e.g., antiprotease alpha-1-antitrypsin) tissue inhibitor of metaloproteinase, antioxidants (e.g., **superoxide dismutase**), enhancers of local host defense (e.g., interferons), mucolytics (e.g., DNase); and proteins which block inflammatory cytokines.

DETDESC:

DETD (36)

The . . . may prove useful is in the development of a gene therapy vector encoding CFTR. As described above, the first generation **adenoviral vector** approaches the maximum packaging capacity for viral DNA encapsidation. As a result, this virus grows poorly and may occassionally give. . .

DETDESC:

DETD (37)

In addition, by expressing only ORF6 of E4, these second generation **adenoviral vectors** may be safer for use in gene therapy. Although ORF6 expression is sufficient for viral DNA replication and late protein.

DETDESC:

DETD (108)

In summary, a mild, transient, pulmonary inflammatory response appears to be associated with the intratracheal administration of the described doses of **adenoviral vector** in the Syrian Hamster.

DETDESC:

DETD (109)

A . . . spread of ineffective viral vectors to organs outside of the

lung and the antibody response of the animals to the **adenoviral vector**. In this study, three treatment groups (vehicle control, low dose virus, high dose virus) each contained 12 animals. Animals.

DETDESC:

DETD(111)

Studies of recombinant adenovirus are also underway in primates. The goal of these studies is to assess the ability of recombinant **adenoviral vectors** to deliver genes to the respiratory epithelium in vivo and to assess the safety of the construct in primates. Initial.

DETDESC:

DETD(233)

Construction and Packaging of Pseudo **Adenoviral Vector** (PAV)

DETDESC:

DETD(237)

For . . . desirable to generate significant quantities of PAV virion free from contaminating helper virus. The primary advantage of PAV over standard **adenoviral vectors** is the ability to package large DNA inserts into virion (up to about 36 kb). However, PAV requires a helper.

DETDESC:

DETD(246)

An **adenoviral vector** is prepared as described in Example 7 while substituting the PGK promoter for the Eta promoter.

DETDESC:

DETD(248)

An **adenoviral vector** is prepared as described in Example 11 while substituting the PGK promoter for the Ad2 major late promoter (MLP).

CLAIMS:

CLMS(1)

We claim:

1. An **adenoviral vector** comprising an adenovirus genome from which one or more of the E4 open reading frames has been deleted, but retaining.

CLAIMS:

CLMS(5)

5. The **adenoviral vector** of claim 1 in which open reading frame 6 of the E4 region is retained in the adenovirus genome.

CLAIMS:

CLMS (6)

6. The **adenoviral vector** of claim 1 in which open reading frame 3 of the E4 region is retained in the adenovirus genome.

CLAIMS:

CLMS (7)

7. The **adenoviral vector** of claim 1 wherein the DNA sequence encodes cystic fibrosis transmembrane regulator protein.

CLAIMS:

CLMS (8)

8. The **adenoviral vector** of claim 2 wherein the DNA sequence encodes cystic fibrosis transmembrane regulator protein.

CLAIMS:

CLMS (9)

9. The **adenoviral vector** of claim 3 wherein the DNA sequence encodes cystic fibrosis transmembrane regulator protein.

CLAIMS:

CLMS (10)

10. The **adenoviral vector** of claim 3 wherein the DNA sequence is inserted into the deleted Ela and Elb regions of the adenoviral genome.

CLAIMS:

CLMS (11)

11. The **adenoviral vector** of claim 5 wherein the DNA sequence encodes cystic fibrosis transmembrane regulator protein.

CLAIMS:

CLMS (12)

12. The **adenoviral vector** of claim 6 wherein a cytomegalovirus promoter is operably linked to the DNA sequence of interest.

CLAIMS:

CLMS (13)

13. . . . to airway epithelial cells of a cystic fibrosis patient comprising administering directly to airway epithelial cells of the patient an **adenoviral vector**, said vector comprising an adenovirus genome from which one or more E4 open reading frames has been deleted, but retaining. . . .

=> d kwic,2

US PAT NO: 5,641,662 :IMAGE AVAILABLE:

L3: 2 of 6

SUMMARY:

BSUM(7)

Retroviruses, . . . . intratracheal (IT), intravenous, intraperitoneal, intramuscular, and arterial injection. Expression of introduced genes, either complexed to cationic vectors or packaged in **adenoviral vectors** has been demonstrated in the lungs of rodents after IT instillation. However, IT injection is invasive and produces a non-uniform. . . .

DETDESC:

DETD(22)

Examples of beneficial therapeutic nucleic acid sequences are those encoding molecules have **superoxide dismutase** activity or catalase activity to protect the lung from oxidant injury; endothelial prostaglandin synthase to produce prostacyclin and prostaglandin E2; . . .

DETDESC:

DETD(72)

Genes . . . prevention of lung damage due to degenerative lung disorders caused by smoking and other environmental agents. For example, genes encoding **superoxide dismutase** (SOD) or catalase, as well as alpha.-1 antitrypsin, will be particularly useful for this purpose. These gene sequences are known.. . . .

=> d kwic, 3

US PAT NO: 5,599,712 :IMAGE AVAILABLE: L3: 3 of 6

SUMMARY:

BSUM(6)

Several . . . and heavy metal cations have been identified. Induction or elevated activities of each of metallothionein (MT), gamma-glutamyl transpeptidase (.gamma.-GTP) and **superoxide dismutase** (SOD) are known to provide resistance to ionizing radiation damage in vitro. Since these proteins function intracellularly to scavenge free. . . . continual levels of the intracellular quantities required to furnish protection against ionizing radiation or an anticancer agent. Furthermore, if metallothionein, **superoxide dismutase** or gamma glutamyl transpeptidase proteins are administered to cells extracellularly, they may be rapidly degraded by proteases and fail to function intracellularly. No method for providing functional intracellular therapeutic levels of metallothionein, **superoxide dismutase** or gamma glutamyl transpeptidase to normal tissues *in vivo* is known.

SUMMARY:

BSUM(12)

Another object of the present invention is to provide intracellular therapeutic quantities of metallothionein, **superoxide dismutase** and/or gamma glutamyl transpeptidase in normal tissues *in vivo* adequate to furnish protection against ionizing radiation or an anticancer agent.

SUMMARY:

BSUM(14)

In . . . proteins of the invention that are capable of neutralizing or eliminating the toxic species can be gamma glutamyl transpeptidase,

manganese **superoxide dismutase**, or metallothionein.

SUMMARY:

BSUM(16)

In . . . of the invention comprises a mixture of polynucleotides selected from a polynucleotide encoding gamma glutamyl transpeptidase, a polynucleotide encoding manganese **superoxide dismutase** or a polynucleotide encoding metallothionein. Alternatively, the pharmaceutical composition of the invention can comprise a polynucleotide encoding gamma glutamyl transpeptidase, a polynucleotide encoding manganese **superoxide dismutase** or a polynucleotide encoding metallothionein.

SUMMARY:

BSUM(18)

Another . . . polynucleotide in such a composition of the invention can be a polynucleotide encoding gamma glutamyl transpeptidase, a polynucleotide encoding manganese **superoxide dismutase** or a polynucleotide encoding metallothionein. The pharmaceutically acceptable vehicle in such a composition of the invention can be a liposome, . . .

DRAWING DESC:

DRWD(4)

FIGS. 3A and 3B are schematic drawings of the construction of a manganese **superoxide dismutase** recombinant adenovirus vector (Ad-MnSOD). FIG. 3A illustrates the Wild-type Adenovirus type 5 (Ad5) genome showing the Ela, Elband E3 regions. . . the appropriate expression cassettes. FIG. 3B illustrates an expression cassette containing regulatory sequences and a recombinant DNA sequence encoding manganese **superoxide dismutase**.

DETDESC:

DETD(4)

The . . . wherein the protein is transiently expressed in the individual. The transgenes of the present invention encode protein(s), such as metallothionein, **superoxide dismutase** or gamma glutamyl transpeptidase, that scavenge a toxic free radical, superoxide anion and/or heavy metal cation.

DETDESC:

DETD(11)

Protection against superoxide radicals requires antioxidants, such as GSH, and the O.<sub>2</sub>.sup.- -scavenging enzyme **superoxide dismutase** (SOD). SODs are metalloenzymes that are essential for dismutation of O.<sub>2</sub>.sup.- to H<sub>2</sub>O<sub>2</sub> and O<sub>2</sub>. There are three forms. . .

DETDESC:

DETD(21)

Viruses . . . multiple copies of the gene of interest into every cell in a culture, thus providing high efficiency transfection *in vivo*. **Adenoviral vectors** provide one useful means for delivering genes *in vivo* because adenoviruses can efficiently infect nondividing cells and

can direct various. . . Vector-mediated gene expression can be achieved in a variety of tissues by administration of a concentrated solution containing the desired **adenoviral vector**. Rosenblum et al., Science 252: 431 (1991); Quantin et al., Proc. Natl. Acad. Sci. USA 89: 2581 (1992); Stratford-Perricaudet et. . .

DETDESC:

DETD(22)

When . . . Natl. Acad. Sci USA 84: 7413 (1987). For transfection of pulmonary epithelium, the method of the present invention preferably utilizes **adenoviral vectors**, lipofection with liposomes or ligand-DNA conjugates.

DETDESC:

DETD(31)

In . . . can be constructed so as to transfer and express, in respiratory epithelium, the DNA encoding either gamma glutamyl transpeptidase, manganese **superoxide dismutase**, metallothionein, a combination of DNA sequences encoding any two of these proteins, or a combination of DNA sequences encoding all. . .

DETDESC:

DETD(34)

A DNA sequence encoding the entire **superoxide dismutase**, preferably MnSOD, coding region is isolated or synthesized by methods well known to the art based on the MnSOD sequences. . .

DETDESC:

DETD(36)

DNA . . . 2 pseudogene 1; :b: ATCC 57152, 57153--bMT-IIA containing the human metallothionein 2 gene; :c: ATCC 20745--pYAS11 containing cDNA encoding human **superoxide dismutase** 1; :d: ATCC 20796--pYLUIGF2-14 containing DNA encoding human **superoxide dismutase** 1; :e: ATCC 39786--pSOD alpha 2 containing DNA encoding human **superoxide dismutase** 1; :f: ATCC 59946, 59947--phMnSOD4 containing DNA encoding human **superoxide dismutase** 2; :g: ATCC 61646, 61647 containing cDNA encoding human **superoxide dismutase** 1; :h: ATCC 86406--IB881 containing cDNA encoding human **superoxide dismutase** or (3) polymerase chain reaction amplification of the desired DNA sequences from the DNA libraries disclosed in the above references. . .

DETDESC:

DETD(41)

A second way to produce the recombinant **adenoviral vector** of the present invention is to coprecipitate a linearized plasmid containing the desired cDNA encoding MT, .gamma.-GTP or MnSOD with. . .

DETDESC:

DETD(42)

Recombinant adenovirus plaques containing the human gamma glutamyl transpeptidase, manganese **superoxide dismutase** and metallothionein protein cDNA (Ad-.gamma.GTP; Ad-MnSOD, and Ad-MT

respectively) are then identified by restriction cleavage, Southern analysis and/or Northern analysis.

DETDESC:

DETD(43)

Each . . . cells. Any tissue of the human body can be targeted for the gene therapy of the present invention using the **adenoviral vectors** described above. These vectors can be introduced by intratracheal, intravenous, intraperitoneal, intramuscular, intrarectal, intravesicle, intraintestinal, intraoral, intraocular or intraarterial injections.

DETDESC:

DETD(57)

Immunohistochemical Detection of the Human Gamma Glutamyl Transpeptidase, Manganese **Superoxide Dismutase** and Metallothionein After In Vivo Infection

DETDESC:

DETD(58)

Human gamma glutamyl transpeptidase, manganese **superoxide dismutase** and metallothionein are evaluated in cytocentrifuge preparations of human lung epithelial lavage samples or lung biopsy samples taken 2 days, . . . or Ad-.gamma.-GTP. The alkaline phosphatase monoclonal anti-alkaline phosphatase method is used with antibodies specific for human gamma glutamyl transpeptidase, manganese **superoxide dismutase** and metallothionein antibody. Cordell et al., J. Histol. Cytochem. 32: 219 (1984).

DETDESC:

DETD(60)

The in vitro or in vivo expressed human gamma glutamyl transpeptidase, manganese **superoxide dismutase** and metallothionein are each tested for their functional activity.

DETDESC:

DETD(71)

Construction of the recombinant **adenoviral vector** Ad-MT and expression of recombinant MT from lung epithelium in vivo

DETDESC:

DETD(76)

Construction of the recombinant **adenoviral vector** Ad-MnSOD and expression of recombinant MnSOD from lung epithelium in vivo

DETDESC:

DETD(81)

Construction of the recombinant **adenoviral vector** Ad-.gamma.-GTP and expression of recombinant .gamma.-GTP from lung epithelium in vivo

CLAIMS:

CLMS (1)

What . . .  
toxic species to provide a protection therefrom and (ii) is selected from a group consisting of gamma glutamyl transpeptidase, manganese **superoxide dismutase**, and metallothionein;  
(B) a pharmaceutically acceptable vehicle for said polynucleotide wherein said vehicle is selected from a liposome and a replication-deficient. . . .

CLAIMS:

CLMS (11)

11. The method of claim 1, wherein said protein is manganese **superoxide dismutase**.

CLAIMS:

CLMS (13)

13. . . . a mixture of polynucleotides selected from the group consisting of a polynucleotide encoding gamma glutamyl transpeptidase, a polynucleotide encoding manganese **superoxide dismutase** and a polynucleotide encoding metallothionein.

CLAIMS:

CLMS (15)

15. The method of claim 1, wherein said pharmaceutical composition comprises a polynucleotide encoding manganese **superoxide dismutase**.

CLAIMS:

CLMS (25)

25. . . .  
with said toxic species to provide protection therefrom and (b) is selected from a group consisting gamma glutamyl transpeptidase, manganese **superoxide dismutase**, and metallothionein; and  
(B) a pharmaceutically acceptable vehicle for said polynucleotide wherein said vehicle is selected from a liposome and. . . .

=> d kwic, 4

US PAT NO: 5,571,797 :IMAGE AVAILABLE: L3: 4 of 6

SUMMARY:

BSUM(13)

Preferably, . . . . a vascular smooth muscle growth factor is platelet derived growth factor (PDGF); and 4) a free radical scavenger is manganese **superoxide dismutase** (MnSOD).

DETDESC:

DETD(45)

Preférable, . . . . a vascular smooth muscle growth factor is platelet derived growth factor (PDGF); and 4) a free radical scavenger is manganese **superoxide dismutase** (MnSOD).

DETDESC:

DETD(48)

TNF may induce radioprotection through the production of manganese **superoxide dismutase** (MnSOD), which has been shown to be associated with radiation resistance in the T-cell line HUT-78 (Wong, et al., 1991) . . .

DETDESC:

DETD(124)

Plasmid . . . about 491 base pair fragment of the Egr-1 promoter operatively linked to an encoding region for the free-radical scavenger manganese **superoxide dismutase** (MnSOD). pE425-MnSOD was constructed from a plasmid nMnSOD #0664 (Genentech) (Wong, 1989) which contains MnSOD cDNA and pE425-CAT, which contains. . .

DETDESC:

DETD(206)

A . . . adeno-associated virus (AAV vectors), such as those described by U.S. Pat. No. 5,139,941, incorporated herein by reference; and, particularly, recombinant **adenoviral vectors**. Techniques for preparing replication-defective infective viruses are well known in the art, as exemplified by Ghosh-Choudhury & Graham (1987); McGrory. . .

=> d kwic,5

US PAT NO: 5,552,309 :IMAGE AVAILABLE: L3: 5 of 6

ABSTRACT:

A process for introducing an expression vehicle (e.g., plasmids, retroviral vectors, **adenoviral vectors**) into cells, which comprises contacting the cells with the expression vehicle and a polyol. The polyol may be a polyoxalkylene. . .

SUMMARY:

BSUM(3)

The . . . 83, pgs. 2007-2011 (1991)), retroviral vectors (Nabel, et al., 1990; Flugelman, et al., Circulation, Vol. 85, pgs. 1110-1117 (1992)) and **adenoviral vectors** (Guzman, et al., Circulation, Vol. 88, pgs. 2838-2848 (1993); Lemarchand, et al., Proc. Nat. Acad. Sci., Vol. 89, pgs. 6482-6486. . .

SUMMARY:

BSUM(4)

Gene delivery vehicles which may be employed include retroviral vectors and **adenoviral vectors**. Retroviral vectors may be employed for infecting dividing cells, while **adenoviral vectors** may be employed for infecting dividing and non-dividing cells. **Adenoviral vectors** have been used successfully for *in vivo* gene transfer of marker genes such as *.beta.-galactosidase* (Stratford-Perricaudet, et al., Hum. Gene. . .

SUMMARY:

BSUM(16)

Expression . . . or, such plasmid vector may be contained within an infectious viral vector particle, such as a retroviral vector particle, an **adenoviral vector** particle, or an adeno-associated virus vector particle.

SUMMARY:

BSUM(17)

In . . . viral vector particle, sometimes hereinafter referred to as a "viral vector." The viral vector may be a retroviral vector, an **adenoviral vector**, an adeno-associated virus vector, or a Herpes Virus vector.

SUMMARY:

BSUM(18)

In one embodiment, the viral vector is an **adenoviral vector**.

SUMMARY:

BSUM(19)

The **adenoviral vector** which is employed may, in one embodiment, be an **adenoviral vector** which includes essentially the complete adenoviral genome (Shenk, et al., Curr. Top. Microbiol. Immunol., 111(3): 1-39 (1984)). Alternatively, the **adenoviral vector** may be a modified **adenoviral vector** in which at least a portion of the adenoviral genome has been deleted.

SUMMARY:

BSUM(20)

In one embodiment, the **adenoviral vector** comprises an adenoviral 5' ITR; an adenoviral 3' ITR; an adenoviral encapsidation signal; and at least one DNA sequence encoding. . . .

SUMMARY:

BSUM(25)

This construct is then used to produce an **adenoviral vector**. Homologous recombination is effected with a modified or mutated adenovirus in which at least the majority of the E1 and. . . . aids in enabling the plasmid vector and modified adenovirus to transfect the helper cells. Upon such homologous recombination, a recombinant **adenoviral vector** is formed that includes DNA sequences derived from the shuttle plasmid between the NotI site and the homologous recombination fragment,. . . .

SUMMARY:

BSUM(28)

In one embodiment, the **adenoviral vector** comprises an adenoviral 5' ITR; an adenoviral 3' ITR; an adenoviral encapsidation signal; and at least one DNA sequence encoding. . . .

SUMMARY:

BSUM(34)

The present invention is particularly applicable to the treatment of diseases of the blood vessel wall. For example, infectious **adenoviral vector** particles will include at least one nucleic acid sequence encoding therapeutic agent for treating a disease of the blood vessel. . . such re-implanted cells express the agent for treating a disease of the blood vessel wall in vivo. For example, the **adenoviral vector** particle may include an antisense c-myb oligonucleotide, which is employed for inhibiting intimal arterial smooth muscle cell accumulation. Other diseases. . .

SUMMARY:

BSUM(35)

Alternatively, the infectious adenoviral particles may be administered in vivo in combination with the polyol, to a host, whereby the infectious **adenoviral vector** particles will infect cells in vivo in a host, thereby providing for in vivo expression of the therapeutic agent in. . . viral particles are administered in an amount effective to produce a therapeutic effect in a host. In one embodiment, the **adenoviral vector** particles may be administered in an amount of from about 1 to about 10.<sup>sup.14</sup> plaque forming units (pfu), preferably from. . . from about 10.<sup>sup.6</sup> to about 10.<sup>sup.10</sup> pfu. The host may be a human or non-human host. The exact dosage of **adenoviral vector** particles which may be administered is dependent upon the age, sex, and weight of the patient, the therapeutic agent which. . .

SUMMARY:

BSUM(36)

The infectious **adenoviral vector** particles and the polyol may be administered systemically, such as, for example, by intravenous or intraperitoneal administration, as well as. . .

SUMMARY:

BSUM(37)

The **adenoviral vector** particles and the polyol may be administered in combination with a physiologically acceptable pharmaceutical carrier. Such pharmaceutical carriers include, but. . .

SUMMARY:

BSUM(38)

DNA sequences encoding therapeutic agents may be placed into the **adenoviral vector** include, but are not limited to, DNA sequences encoding tumor necrosis factor (TNF) genes, such as TNF-.alpha.; genes encoding interferons. . . of hepatitis B or hepatitis non-A non-B virus; antisense c-myb oligonucleotides; and antioxidants such as, but not limited to, manganese **superoxide dismutase** (Mn-SOD), catalase, copper-zinc-**superoxide dismutase** (CuZn-SOD), extracellular **superoxide dismutase** (EC-SOD), and glutathione reductase; tissue plasminogen activator (tPA); urinary plasminogen activator (urokinase); hirudin; nitric oxide synthetase; vasoactive peptides; and angiogenic. . .

DRAWING DESC:

DRWD(4)

FIG. 2 is a schematic of the construction of an **adenoviral vector** including an ITR, an encapsidation signal, a Rous Sarcoma

.. Virus promoter, and an adenoviral tripartite leader (TPL) sequence;

DETDESC:

DETD(5)

The **adenoviral vector** used in this example was a replication deficient Ela/E1b.sup.-, E3.sup.- deletion mutant expressing a nuclear-targeted .beta.-galactosidase gene under the control. . . .

DETDESC:

DETD(13)

The recombinant, replication-deficient **adenoviral vector** Av1Lac Z4, which expresses a nuclear-targetable B-galactosidase enzyme, was constructed in two steps. First, a transcriptional unit consisting of DNA. . . .

DETDESC:

DETD(14)

The . . . was isolated by agarose gel electrophoresis and purified. The ClaI fragment was used as the backbone for all first generation **adenoviral vectors**, and the vectors derived from it are known as Av1.

DETDESC:

DETD(18)

**Adenoviral vector** morphology and integrity were evaluated by high-resolution scanning electron microscopy. Briefly, bovine aortic smooth muscle cells were plated on silicon. . . .

CLAIMS:

CLMS(5)

5. The process of claim 1 wherein said viral particle is an **adenoviral vector** particle.

CLAIMS:

CLMS(13)

13. The composition of claim 9 wherein said viral vector is an **adenoviral vector** particle.

=> d kwic, 6

US PAT NO: 5,496,731 :IMAGE AVAILABLE: L3: 6 of 6

SUMMARY:

BSUM(73)

In . . . may be any host cell-compatible vector. The vector is preferably selected from the group consisting of a retroviral vector, an **adenoviral vector** and a herpesviral vector.

DETDESC:

DETD(135)

In . . . al., *J Biotechniques*, 6:682-690). Proteins such as erythrocyte anion **transporter** (Newton, A. C. and Huestis, W. H., *Biochemistry*, 1988, 27:4655-4659), **superoxide dismutase** and catalase (Tanswell, A. K. et al., 1990, *Biochmica et Biophysica Acta*, 1044:269-274), and UV-DNA repair enzyme (Ceccoll, J. et. . .).

CLAIMS:

CLMS (5)

5. . . . vector according to claim 3 wherein said viral vector is selected from a group consisting of a retroviral vector, an **adenoviral vector**, and a herpesviral vector.

=> d fro,1-6

US PAT NO: 5,670,488 :IMAGE AVAILABLE: L3: 1 of 6  
DATE ISSUED: Sep. 23, 1997  
TITLE: Adenovirus vector for gene therapy  
INVENTOR: Richard J. Gregory, Carlsbad, CA  
              Donna Armentano, Watertown, MA  
              Larry A. Couture, Framingham, MA  
              Alan E. Smith, Wellesley, MA  
ASSIGNEE: Genzyme Corporation, Framingham, MA (U.S. corp.)  
APPL-NO: 08/136,742  
DATE FILED: Oct. 13, 1993  
REL-US-DATA: Continuation-in-part of Ser. No. 985,478, Dec. 3, 1992,  
              abandoned.  
INT-CL: :6: A61K 48/00; C12N 15/00  
US-CL-ISSUED: 514/44; 424/93.2; 435/320.1; 935/62  
US-CL-CURRENT: 514/44; 424/93.2; 435/320.1; 935/62  
SEARCH-FLD: 435/320.1; 514/44; 424/93.2; 935/62  
REF-CITED:

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93 19191	9/1993	World Intellectual Property Organization

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ART-UNIT: 189

PRIM-EXMR: Deborah Crouch

LEGAL-REP: Brumbaugh, Graves Donohue & Raymond

ABSTRACT:

Gene Therapy vectors, which are especially useful for cystic fibrosis, and methods for using the vectors are disclosed.

US PAT NO: 5,641,662 :IMAGE AVAILABLE: L3: 2 of 6  
 DATE ISSUED: Jun. 24, 1997  
 TITLE: Transfection of lung via aerosolized transgene delivery  
 INVENTOR: Robert James Debs, Mill Valley, CA  
 Ning Zhu, El Cerrito, CA  
 ASSIGNEE: The Regents of the University of California, Oakland, CA  
 (U.S. corp.)  
 APPL-NO: 08/029,022  
 DATE FILED: Mar. 10, 1993  
 REL-US-DATA: Continuation-in-part of Ser. No. 972,135, Nov. 5, 1992,  
                   which is a continuation-in-part of Ser. No. 809,291,  
                   Dec. 17, 1991, abandoned.  
 INT-CL: :6: C12N 15/64; C12N 15/87; A61K 48/00; A61K 9/127  
 US-CL-ISSUED: 435/172.1, 172.3, 320.1; 424/450; 514/44; 128/200.14,  
                   200.24; 536/24.1; 436/71  
 US-CL-CURRENT: 435/172.1; 128/200.14, 200.24; 424/450; 435/172.3, 320.1;  
                   436/71; 514/44; 536/24.1  
 SEARCH-FLD: 514/44; 424/450; 435/172.1, 172.3, 320.1; 935/62, 54, 55;  
                   128/200.14, 200.24; 536/24.1; 436/71  
 REF-CITED:

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5,264,618	11/1993	Felgner et al.	560/224

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WO91/17773	11/1991	World Intellectual Property Organization

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ART-UNIT: 184

PRIM-EXMR: Charles C. P. Rories

LEGAL-REP: Townsend and Townsend and Crew

ABSTRACT:

Methods and compositions for producing a mammal capable of expressing an exogenously supplied gene in cells of the airway are disclosed. Lipid carrier-nucleic acid complexes are prepared then delivered via aerosol to the lung airway. The invention provides a direct method for transforming pulmonary cells as a means for treating disorders of the lung as for providing a means for delivering substances systematically following expression in the lung.

15 Claims, 45 Drawing Figures

US PAT NO: 5,599,712 :IMAGE AVAILABLE: L3: 3 of 6  
DATE ISSUED: Feb. 4, 1997  
TITLE: Protection from ionizing irradiation or chemotherapeutic drug damage by in vivo gene therapy  
INVENTOR: Joel S. Greenberger, Sewickley, PA  
ASSIGNEE: University of Pittsburgh, Pittsburgh, PA (U.S. corp.)  
APPL-NO: 08/136,079  
DATE FILED: Oct. 15, 1993  
INT-CL: :6: A61K 48/00; C12N 15/00  
US-CL-ISSUED: 435/267, 320.1; 514/44; 424/93.21, 93.2  
US-CL-CURRENT: 435/267; 424/93.2, 93.21; 435/320.1; 514/44  
SEARCH-FLD: 514/44, 2; 435/172.3, 320.1, 172.1, 172.2, 172.3, 172.4; 424/94.1, 94.3, 94.4, 93.1, 93.21  
REF-CITED:

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ART-UNIT: 184  
PRIM-EXMR: Jacqueline M. Stone  
ASST-EXMR: Andrew Milne  
LEGAL-REP: Foley & Lardner

ABSTRACT:

A method of protecting a subject against an agent that elicits production of toxic free radicals, superoxide anions, or heavy metal cations in the subject consisting of the in vivo administration to the subject of a polynucleotide encoding a protein that is transiently expressed in said subject. The transiently expressed protein is capable of neutralizing or eliminating the toxic free radicals, superoxide anions or heavy metal cations that are elicited by the agent. This method is particularly

useful in protecting cancer patients against the damaging effects of ionizing radiation and/or chemotherapeutic drugs.

25 Drawing Figures

US PAT NO: 5,571,797 :IMAGE AVAILABLE: L3: 4 of 6  
DATE ISSUED: Nov. 5, 1996  
TITLE: Method of inducing gene expression by ionizing radiation  
INVENTOR: Tsuneya Ohno, Boston, MA  
Ralph R. Weichselbaum, Chicago, IL  
Donald W. Kufe, Wellesley, MA  
ASSIGNEE: Arch Development Corporation, Chicago, IL (U.S. corp.)  
APPL-NO: 08/241,863  
DATE FILED: May 11, 1994  
INT-CL: :6: A61K 48/00; A61K 51/00  
US-CL-ISSUED: 514/44; 424/1.11, 1.49, 1.61, 1.65, 1.69, 450, 93.2,  
93.21; 435/172.3, 320.1, 69.1, 69.5; 536/24.1; 935/6,  
34, 59, 62  
US-CL-CURRENT: 514/44; 424/1.11, 1.49, 1.61, 1.65, 1.69, 93.2, 93.21,  
450; 435/69.1, 69.5, 172.3, 320.1; 536/24.1; 935/6, 34,  
59, 62  
SEARCH-FLD: 424/1.11, 1.29, 1.37, 1.49, 1.57, 450, 93.2, 93.21;  
435/172.3, 320.1, 69.1, 69.5; 514/44; 536/23.1, 23.2,  
23.5, 23.51, 23.52, 24.1, 23.7; 935/36, 62, 6, 34, 59  
REF-CITED:

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WO94/06916 3/1994 World Intellectual Property Organization

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ART-UNIT: 184

PRIM-EXMR: Bruce R. Campell

LEGAL-REP: Arnold White & Durkee

ABSTRACT:

The present invention provides a method for delivering ionizing radiation to specific tissues, resulting in the activation of a DNA molecule comprising a radiation responsive enhancer-promoter operatively linked to an encoding region that encodes at least one polypeptide. The radiation source may generally be in the form of a radionuclide, capable of gamma or beta emissions. Processes for regulating polypeptide expression and inhibiting tumor growth using such DNA molecules are also provided.

16 Claims, 3 Drawing Figures

US PAT NO: 5,552,309 :IMAGE AVAILABLE: L3: 5 of 6

DATE ISSUED: Sep. 3, 1996

TITLE: Use of polyols for improving the introduction of genetic material into cells

INVENTOR: Keith L. March, Carmel, IN

ASSIGNEE: Indiana University Foundation, Bloomington, IN (U.S. corp.)

APPL-NO: 08/315,974  
DATE FILED: Sep. 26, 1994  
INT-CL: :6: C12N 63/00; C12N 5/00; C12N 15/00  
US-CL-ISSUED: 435/172.3, 235.1, 240.2, 320.1; 514/44; 424/93.1, 93.2,  
426; 935/57  
US-CL-CURRENT: 435/172.3; 424/93.1, 93.2, 426; 435/235.1, 320.1; 514/44;  
935/57  
SEARCH-FLD: 424/93.1, 93.2, 426; 435/172.3, 320.1, 240.2; 514/44;  
935/57

## REF-CITED:

U.S. PATENT DOCUMENTS			
5,118,512	6/1992	O'Leary et al.	424/549
5,298,222	3/1994	O'Leary et al.	422/28

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Smith, et al., Nature Genetics, vol. 5, pp. 397-401 (Dec. 1993).  
Yei, et al., Human Gene Therapy, vol. 5, pp. 731-744 (1994).  
ART-UNIT: 184  
PRIM-EXMR: Bruce R. Campell  
LEGAL-REP: Elliot M. Olstein, Raymond J. Lillie

## ABSTRACT:

A process for introducing an expression vehicle (e.g., plasmids, retroviral vectors, **adenoviral vectors**) into cells, which comprises contacting the cells with the expression vehicle and a polyol. The polyol may be a polyoxalkylene block copolymer, such as a polyoxypropylene-polyoxyethylene block copolymer. The use of the polyol provides for greater efficiency of transduction of the expression vehicle.

15 Claims, 9 Drawing Figures

US PAT NO: 5,496,731 :IMAGE AVAILABLE: L3: 6 of 6  
DATE ISSUED: Mar. 5, 1996  
TITLE: Broad-spectrum tumor suppressor genes, gene products and methods for tumor suppressor gene therapy  
INVENTOR: Hong-Ji Xu, 10 Moonseed Pl., The Woodlands, TX 77381  
Shi-Xue Hu, 10 Moonseed Pl., The Woodlands, TX 77381  
William F. Benedict, 21 E. Wedgewood Glen, The Woodlands,  
TX 77381  
APPL-NO: 08/038,760  
DATE FILED: Mar. 25, 1993  
INT-CL: :6: C12N 15/86; C12N 15/85  
US-CL-ISSUED: 435/320.1; 536/23.5; 514/44  
US-CL-CURRENT: 435/320.1; 514/44; 536/23.5  
SEARCH-FLD: 536/350, 23.5; 435/69.1, 320.1

## REF-CITED:

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5,174,993	6/1990	Paoletti	424/199.1

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0259031	8/1987	European Patent Office
WO88/09387	5/1988	World Intellectual Property Organization
WO89/03429	8/1988	World Intellectual Property Organization
WO89/06703	1/1989	World Intellectual Property Organization
WO90/05180	10/1989	World Intellectual Property Organization
WO90/12807	4/1990	World Intellectual Property Organization
WO91/15580	4/1991	World Intellectual Property Organization
WO92/05272	9/1991	World Intellectual Property Organization

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- Zhou et al., 1993, Characterization of RB+ clones of RB reconstituted retinoblastoma and osteosarcoma cells, Proc. Am. Assoc. Cancer Res. 34:538 abstract No. 3214.
- ART-UNIT: 185
- PRIM-EXMR: Richard A. Schwartz
- ASST-EXMR: David B. Schmickel
- ABSTRACT:**
- The present invention relates to a broad-spectrum tumor suppressor gene and the protein expressed by that gene in appropriate host cells. The protein is a second in-frame AUG codon-initiated retinoblastoma protein of about 94 kD relative molecular mass. The present invention also relates to methods of treating a mammal having a disease or disorder characterized by abnormal cellular proliferation, such as a tumor or cancer and methods of treating abnormally proliferating cells, such as tumor or cancer cells. Treatment is accomplished by inserting a host cell compatible p94.sup.RB expression vector or an effective amount of p94.sup.RB protein into a cell or cells in need of treatment.

12 Claims, 26 Drawing Figures



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**HIGHLIGHT set on as ''**  
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51318 SUPEROXIDE DISMUTASE?  
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09165977 97298020  
Intrastriatal grafts of embryonic mesencephalic rat neurons genetically modified using an **adenovirus** encoding human Cu/Zn superoxide dismutase.  
Barkats M; Nakao N; Grasbon-Frodl EM; Bilang-Bleuel A; Revah F; Mallet J; Brundin P  
Laboratoire de Genetique Moleculaire de la Neurotransmission et des Processus Neurodegeneratifs, UMR CNRS C9923, Hopital de la Pitie Salpetriere, Paris, France.  
Neuroscience (UNITED STATES) Jun 1997, 78 (3) p703-13, ISSN 0306-4522  
Journal Code: NZR  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

- end of record -

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Display 2/3/2 (Item 2 from file: 154)  
DIALOG(R)File 154: MEDLINE(R)  
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09058853 97238105  
Ca<sup>2+</sup> and reactive oxygen species in staurosporine-induced neuronal apoptosis.

Prehn JH; Jordan J; Shadage GD; Preis E; Galindo MF; Boos RP; Krieglstein J; Miller RJ  
Department of Pharmacology and Toxicology, Philipps University, Marburg, Germany.

J Neurochem (UNITED STATES) Apr 1997, 68 (4) p1679-85, ISSN 0022-3042  
Journal Code: JAV  
Contract/Grant No.: MH40165, MH, NIMH; NS21442, NS, NINDS  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

- end of record -

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Display 2/3/3 (Item 3 from file: 154)  
DIALOG(R) File 154: MEDLINE(R)  
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08838139 97059139  
Superoxide-mediated actin response in post-hypoxic endothelial cells.  
Crawford LE; Milliken EE; Irani K; Zweier JL; Becker LC; Johnson TM;  
Eissa NT; Crystal RG; Finkel T; Goldschmidt-Clermont PJ  
Division of Cardiology, Department of Medicine, The Johns Hopkins  
University School of Medicine, Baltimore, Maryland 21205, USA.  
J Biol Chem (UNITED STATES) Oct 25 1996, 271 (43) p26863-7, ISSN  
0021-9258 Journal Code: HIV  
Contract/Grant No.: HL52315, HL, NHLBI  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

- end of record -

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Display 2/3/4 (Item 4 from file: 154)  
DIALOG(R) File 154: MEDLINE(R)  
(c) format only 1997 Knight-Ridder Info. All rts. reserv.

08776986 96290653  
An **adenovirus** encoding CuZnSOD protects cultured striatal neurones  
against glutamate toxicity.  
Barkats M; Bemelmans AP; Geoffroy MC; Robert JJ; Loquet I; Horellou P;  
Revah F; Mallet J  
Laboratoire mixte Rhone-Poulenc-RORER/CNRS C9923, CERVI, Hopital de la  
Pitie Salpetriere, Paris, France.  
Neuroreport (ENGLAND) Jan 31 1996, 7 (2) p497-501, ISSN 0959-4965  
Journal Code: A6M  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

- end of record -

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Display 2/3/5 (Item 5 from file: 154)  
DIALOG(R) File 154: MEDLINE(R)  
(c) format only 1997 Knight-Ridder Info. All rts. reserv.

08607307 96239197  
Mechanisms of unusually high antioxidant activity of RSV-SR-transformed  
cells and of its suppression by activated p21ras.  
Deichman GI; Kashkina LM; Mizenina OA; Gorojanskaya EG; Nikiforov MA;  
Gudkov AV; Dyakova NA; Komelkov AV; Prilutskaya MO; Kushlinsky NE; Tatosyan  
AG  
Institute of Carcinogenesis, Cancer Research Center of Russian Academy of  
Medical Sciences, Moscow, Russia.  
Int J Cancer (UNITED STATES) Jun 11 1996, 66 (6) p747-52, ISSN  
0020-7136 Journal Code: GQU

Contract/Grant No.: R21 CA62045, CA, NCI  
Languages: ENGLIS  
Document type: JOURNAL ARTICLE

- end of record -

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Display 2/3/6 (Item 6 from file: 154)  
DIALOG(R) File 154: MEDLINE (R)  
(c) format only 1997 Knight-Ridder Info. All rts. reserv.

08593249 96226070

Protective effect of transforming growth factor-beta 1 on beta-amyloid neurotoxicity in rat hippocampal neurons.

Prehn JH; Bindokas VP; Jordan J; Galindo MF; Ghadge GD; Roos RP; Boise LH ; Thompson CB; Krajewski S; Reed JC; Miller RJ

Department of Pharmacological and Physiological Sciences, University of Chicago, Illinois 60637, USA.

Mol Pharmacol (UNITED STATES) Feb 1996, 49 (2) p319-28, ISSN 0026-895X Journal Code: NGR

Contract/Grant No.: DA02121, DA, NIDA; DA02575, DA, NIDA; MH40165, MH, NIMH; +

Languages: ENGLISH

Document type: JOURNAL ARTICLE

- end of record -

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Display 2/3/7 (Item 7 from file: 154)  
DIALOG(R) File 154: MEDLINE (R)  
(c) format only 1997 Knight-Ridder Info. All rts. reserv.

08306402 95327064

Expression of human copper/zinc-superoxide dismutase inhibits the death of rat sympathetic neurons caused by withdrawal of nerve growth factor.

Jordan J; Ghadge GD; Prehn JH; Toth PT; Roos RP; Miller RJ

Department of Pharmacological and Physiological Sciences, University of Chicago, Illinois 60637, USA.

Mol Pharmacol (UNITED STATES) Jun 1995, 47 (6) p1095-1100, ISSN 0026-895X Journal Code: NGR

Contract/Grant No.: DA02575, DA, NIDA; DA02121, DA, NIDA; MH40165, MH, NIMH; +

Languages: ENGLISH

Document type: JOURNAL ARTICLE

- end of record -

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Display 2/3/8 (Item 8 from file: 154)  
DIALOG(R) File 154: MEDLINE (R)  
(c) format only 1997 Knight-Ridder Info. All rts. reserv.

07054168 91346113

The E1b oncogene of **adenovirus** confers cellular resistance to cytotoxicity of tumor necrosis factor and monoclonal anti-Fas antibody.

Hashimoto S; Ishii A; Yonehara S

Meiji Institute of Health Science, Odawara, Japan.

Int Immunol (ENGLAND) Apr 1991, 3 (4) p343-51, ISSN 0953-8178  
Journal Code: AY5

Languages: ENGLISH

Document type: JOURNAL ARTICLE

- end of record -

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Display 2/3/9 (Item 9 from file: 154)  
DIALOG(R) File 154 (R)  
(c) format only 1997 Knight-Ridder Info. All rts. reserv.

05577541 89077686

Melanin synthesis and the action of L-dopa and 3,4-dihydroxybenzylamine in human melanoma cells.

Kable EP; Parsons PG  
Queensland Institute of Medical Research, Herston, Australia.  
Cancer Chemother Pharmacol (GERMANY, WEST) 1989, 23 (1) p1-7, ISSN  
0344-5704 Journal Code: C9S  
Languages: ENGLISH  
Document type: JOURNAL ARTICLE

- end of record -

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Display 2/3/10 (Item 1 from file: 73)  
DIALOG(R) File 73:EMBASE  
(c) 1997 Elsevier Science B.V. All rts. reserv.

10153072 EMBASE No: 96339142

**Adenovirus** for neurodegenerative diseases: In vivo strategies and ex vivo gene therapy using human neural progenitors  
Sabate O.; Barkats M.; Buc-Caron M.-H.; Castel-Barthe M.-N.; Finiels F.; Horellou P.; Revah F.; Mallet J.  
CNRS C 9923, LGMNPD (LGN), Hopital de la Pitie, 83 Boulevard de l'Hopital, 75013 Paris France  
Clinical Neuroscience (USA) , 1995/96, 3/5 (317-321) CODEN: CINUE  
ISSN: 1065-6766  
LANGUAGES: English SUMMARY LANGUAGES: English

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Display 2/3/11 (Item 2 from file: 73)  
DIALOG(R) File 73:EMBASE  
(c) 1997 Elsevier Science B.V. All rts. reserv.

5901081 EMBASE No: 85146591

Modification of dopa toxicity in human tumour cells  
Parsons P.G.  
Queensland Institute of Medical Research, Herston, Qld. 4006 USA  
BIOCHEM. PHARMACOL. (ENGLAND) , 1985, 34/10 (1801-1807) CODEN: BCPCA  
LANGUAGES: ENGLISH

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Display 2/3/12 (Item 3 from file: 73)  
DIALOG(R) File 73:EMBASE  
(c) 1997 Elsevier Science B.V. All rts. reserv.

1210120 EMBASE No: 78390333

Properties and products of the degradation of DNA by bleomycin and iron (II)  
Sausville E.A.; Stein R.W.; Peisach J.; Horwitz S.B.  
Dept. Molec. Pharmacol., Albert Einstein Coll. Med., Bronx, N.Y. 10461 USA  
BIOCHEMISTRY (WASH.) (USA) , 1978, 17/14 (2746-2754) CODEN: BICHA  
LANGUAGES: ENGLISH

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Display 2/3/13 (Item 1 from file: 71)  
DIALOG(R) File 71:ELSEVIER BIOBASE  
(c) 1997 Elsevier Science B.V. All rts. reserv.

00743074 97249226  
Mutant superoxide dismutase-1-linked familial amyotrophic lateral sclerosis: Molecular mechanisms of neuronal death and protection  
Ghadge G.D.; Lee J.P.; Bindokas V.P.; Jordan J.; Ma L.; Miller R.J.; Roos R.P.  
ADDRESS: Dr. R.P. Roos, Department of Neurology, MC 2030, University of Chicago, 5841 South Maryland Avenue, Chicago, IL 60637, United States  
Journal: Journal of Neuroscience, 17/22 (8756-8766), 1997, United States  
CODEN: JNRSD  
ISSN: 0270-6474  
DOCUMENT TYPE: Article  
LANGUAGES: English SUMMARY LANGUAGES: English  
NO. OF REFERENCES: 40

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Display 2/3/14 (Item 2 from file: 71)  
DIALOG(R) File 71:ELSEVIER BIOBASE  
(c) 1997 Elsevier Science B.V. All rts. reserv.  
00572240 97075064  
Casup 2<sup>sup</sup> + and reactive oxygen species in staurosporine-induced neuronal apoptosis  
Prehn J.H.M.; Jordan J.; Ghadge G.D.; Preis E.; Galindo M.F.; Roos R.P.; Kriegstein J.; Miller R.J.  
ADDRESS: Dr. J.H.M. Prehn, Pharmacology/Toxicology Department, Philipps-University, Ketzerbach 63, 35032 Marburg, Germany  
Journal: Journal of Neurochemistry, 68/4 (1679-1685), 1997, United States  
CODEN: JONRA  
ISSN: 0022-3042  
DOCUMENT TYPE: Article  
LANGUAGES: English SUMMARY LANGUAGES: English  
NO. OF REFERENCES: 52

- end of record -

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Display 2/3/15 (Item 1 from file: 315)  
DIALOG(R) File 315:ChemEng & Biotec Abs  
(c) 1997 RoySocChm, DECHEMA, FizChemie. All rts. reserv.

404436 CEABA Accession No.: 28-01-001636 DOCUMENT TYPE: Patent  
Title: **Adenovirus** including a gene coding for a superoxide dismutase.  
AUTHOR: Barkats, M. ; Mallet, J. ; Perricaudet, M. ; Revah, F.  
CORPORATE SOURCE: Rhone-Poulenc Rorer S.A. F-92160 Antony France  
CODEN: PIXXD2  
PATENT NUMBER: WO 9600790  
PUBLICATION DATE: 11 Jan 1996 (960111) LANGUAGE: English  
PRIORITY PATENT APPLICATION(S) & DATE(S): FR 9408029 (940629)

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Display 2/3/16 (Item 1 from file: 434)  
DIALOG(R) File 434:Scisearch(R) Cited Ref Sci  
(c) 1997 Inst for Sci Info. All rts. reserv.

12214631 Genuine Article#: KV111 No. References: 60  
Title: HIV-1 PROMOTER ACTIVATION FOLLOWING AN OXIDATIVE STRESS MEDIATED BY

SINGLET OXYGEN

Author(s): LEGRAND J; HOEBEKE M; VAIRA D; RENTIERE PIETTE J

Corporate Source: UNIV LIEGE, INST PATHOL B23, VIROL LAB/B-4000

LIEGE//BELGIUM//; UNIV LIEGE, INST PATHOL B23, VIROL LAB/B-4000

LIEGE//BELGIUM//; UNIV LIEGE, INST PHYS B5/B-400 LIEGE//BELGIUM//

Journal: JOURNAL OF PHOTOCHEMISTRY AND PHOTOBIOLOGY B-BIOLOGY, 1993, V17,  
N3 (MAR), P229-237

ISSN: 1011-1344

Language: ENGLISH Document Type: ARTICLE (Abstract Available)

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? s gene therapy and fail? and review?

Processing  
Processed 10 of 56 files ...

Processing  
Processed 20 of 56 files ...

Processing  
Processed 40 of 56 files ...

Completed processing all files

35499 GENE THERAPY

2399694 FAIL?

5411978 REVIEW?

S3 163 GENE THERAPY AND FAIL? AND REVIEW?

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Processed 40 of 56 files ...

Processing  
Completed processing all files

163 S3

122788 ADENOVIR?

S4 27 S3 AND ADENOVIR?

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>>>Duplicate detection is not supported for File 42.  
>>>Duplicate detection is not supported for File 140.  
>>>Duplicate detection is not supported for File 187.  
>>>Duplicate detection is not supported for File 189.  
>>>Duplicate detection is not supported for File 286.  
>>>Duplicate detection is not supported for File 428.  
>>>Duplicate detection is not supported for File 429.  
>>>Duplicate detection is not supported for File 441.  
>>>Duplicate detection is not supported for File 446.  
>>>Duplicate detection is not supported for File 449.  
>>>Duplicate detection is not supported for File 452.  
>>>Duplicate detection is not supported for File 455.  
>>>Duplicate detection is not supported for File 456.

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...completed examining records

S5 23 RD S4 (unique items)

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Display 5/3/1 (Item 1 from file: 73)

DIALOG(R)File 73:EMBASE

(c) 1997 Elsevier Science B.V. All rts. reserv.

10503808 EMBASE No: 97313634

Gene therapy for renal diseases

Lien Y.-H.; Lai L.-W.

Dr. Y.-H. Lien, Section of Renal Disease, Department of Medicine, Univ. of Arizona Hlth. Sci. Center, Tucson, AZ 85724 USA

Kidney International, Supplement (USA) , 1997, 51/61 (S-85-S-88) CODEN: KISUD ISSN: 0098-6577

DOCUMENT TYPE: Journal

LANGUAGES: English SUMMARY LANGUAGES: English

NUMBER OF REFERENCES: 35

- end of record -

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Display 5/3/1 (Item 2 from file: 73)  
DIALOG(R) File 73:EMBASE  
(c) 1997 Elsevier Science B.V. All rts. reserv.

10260610 EMBASE No: 97072654  
Genetic therapy: Past, present, and future  
Flotte T.R.; Ferkol T.W.  
USA  
Pediatric Clinics of North America (USA) , 1997, 44/1 (153-178) CODEN:  
PCNAA ISSN: 0031-3955  
DOCUMENT TYPE: Journal  
LANGUAGES: English SUMMARY LANGUAGES: English  
NUMBER OF REFERENCES: 183

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Display 5/3/3 (Item 3 from file: 73)  
DIALOG(R) File 73:EMBASE  
(c) 1997 Elsevier Science B.V. All rts. reserv.

10157803 EMBASE No: 96313015  
Gene therapy in the United States: A five-year status report  
Ross G.; Erickson R.; Knorr D.; Motulsky A.G.; Parkman R.; Samulski J.;  
Straus S.E.; Smith B.R.  
Yale University School of Medicine, 333 Cedar Street, New Haven, CT  
06520-8035 USA  
Human Gene Therapy (USA) , 1996, 7/14 (1781-1790) CODEN: HGTHE ISSN:  
1043-0342  
LANGUAGES: English SUMMARY LANGUAGES: English

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Display 5/3/4 (Item 4 from file: 73)  
DIALOG(R) File 73:EMBASE  
(c) 1997 Elsevier Science B.V. All rts. reserv.

10119095 EMBASE No: 96310110  
Molecular therapy for renal diseases  
Lipkowitz M.S.; Klotman M.E.; Bruggeman L.A.; Nicklin P.; Hanss B.;  
Rappaport J.; Klotman P.E.  
Department of Medicine, Mount Sinai School of Medicine, Box 1243, One  
Gustave Levy Place, New York, NY 10029 USA  
American Journal of Kidney Diseases (USA) , 1996, 28/4 (475-492) CODEN:  
AJKDD ISSN: 0272-6386  
LANGUAGES: English SUMMARY LANGUAGES: English

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Display 5/3/5 (Item 5 from file: 73)  
DIALOG(R) File 73:EMBASE  
(c) 1997 Elsevier Science B.V. All rts. reserv.

9813801 EMBASE No: 95366288  
Gene therapy for cystic fibrosis: Challenges and future directions  
Wilson J.M.  
Institute for Human Gene Therapy, 204 Wistar Institute, 3601 Spruce St.,  
Philadelphia, PA 19104-4268 USA  
Journal of Clinical Investigation (USA) , 1995, 96/6 (2547-2554) CODEN:  
JCINA ISSN: 0021-9738  
LANGUAGES: English

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Display 5/3/6 (Item 6 from file: 73)  
DIALOG(R) File 73:EMBASE  
(c) 1997 Elsevier Science B.V. All rts. reserv.

9504176 EMBASE No: 95075954  
Gene therapy for cystic fibrosis using cationic liposome mediated gene transfer: A phase I trial of safety and efficacy in the nasal airway  
Sorscher E.J.; Logan A.J.; Frizzell R.A.; Lyrene R.K.; Bebok Z.; Dong J.Y.; Duvall M.D.; Felgner P.L.; Matalon S.; Walker L.; Wiatrak B.J.  
University of Alabama at Birmingham, Children's Hospital of Alabama, Birmingham, AL USA  
Human Gene Therapy (USA) , 1994, 5/10 (1259-1270) CODEN: HGTHE ISSN: 1043-0342  
LANGUAGES: English SUMMARY LANGUAGES: English

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Display 5/3/7 (Item 7 from file: 73)  
DIALOG(R) File 73:EMBASE  
(c) 1997 Elsevier Science B.V. All rts. reserv.

9193736 EMBASE No: 94146724  
The molecular and cellular biology of heart **failure**  
Carter L.F.; Rubin S.A.  
Cardiology (111c), Veterans Admin Medical Center, 5901 East Seventh Street, Long Beach, CA 90822 USA  
CURR. OPIN. CARDIOL. (United Kingdom) , 1994, 9/3 (264-271) CODEN: COPCE ISSN: 0268-4705  
LANGUAGES: English SUMMARY LANGUAGES: English

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Display 5/3/8 (Item 8 from file: 73)  
DIALOG(R) File 73:EMBASE  
(c) 1997 Elsevier Science B.V. All rts. reserv.

9169006 EMBASE No: 94116344  
Coronary restenosis and gene therapy  
Mazur W.; Ali N.M.; Raizner A.E.; French B.A.  
Section of Cardiology, Department of Medicine, Baylor College of Medicine, One Baylor Plaza, Houston, TX 77030 USA  
TEX. HEART INST. J. (USA) , 1994, 21/1 (104-111) CODEN: THIJD ISSN: 0730-2347  
LANGUAGES: English SUMMARY LANGUAGES: English

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Display 5/3/9 (Item 1 from file: 71)  
DIALOG(R) File 71:ELSEVIER BIOBASE  
(c) 1997 Elsevier Science B.V. All rts. reserv.

00738840 97243664  
Prevention of vein graft **failure**: Potential applications for gene therapy  
Baker A.H.; Mehta D.; George S.J.; Angelini G.D.  
ADDRESS: A.H. Baker, Bristol Heart Institute, Bristol Royal Infirmary, Bristol BS2 8HW, United Kingdom  
EMAIL: a.h.baker@bristol.ac.uk

Journal: Cardiovascular Research, 35/3 (442-450), 1997, Netherlands  
CODEN: CVREA  
ISSN: 0008-6363  
PUBLISHER ITEM IDENTIFIER: S0008636397001168  
DOCUMENT TYPE: Review  
LANGUAGES: English SUMMARY LANGUAGES: English  
NO. OF REFERENCES: 74

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Display 5/3/10 (Item 1 from file: 149)  
DIALOG(R) File 149:IAC(SM) Health&Wellness DB(SM)  
(c) 1997 Info Access Co. All rts. reserv.

01679020 SUPPLIER NUMBER: 19230136 (USE FORMAT 7 OR 9 FOR FULL TEXT)  
Lung cancer. (Science, Medicine, and the Future)  
Sethi, Tariq  
British Medical Journal, v314, n7081, p652(4)  
March 1, 1997  
PUBLICATION FORMAT: Magazine/Journal ISSN: 0959-8146 LANGUAGE: English  
RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Professional  
WORD COUNT: 2801 LINE COUNT: 00245

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Display 5/3/11 (Item 2 from file: 149)  
DIALOG(R) File 149:IAC(SM) Health&Wellness DB(SM)  
(c) 1997 Info Access Co. All rts. reserv.

01676744 SUPPLIER NUMBER: 17715890 (USE FORMAT 7 OR 9 FOR FULL TEXT)  
Development and application of herpes simplex virus vectors for human gene therapy.  
Glorioso, J.C.; DeLuca, N.A.; Fink, D.J.  
Annual Review of Microbiology, v49, p675(36)  
Annual, 1995  
PUBLICATION FORMAT: Magazine/Journal ISSN: 0066-4227 LANGUAGE: English  
RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Academic  
WORD COUNT: 16425 LINE COUNT: 01336

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Display 5/3/12 (Item 3 from file: 149)  
DIALOG(R) File 149:IAC(SM) Health&Wellness DB(SM)  
(c) 1997 Info Access Co. All rts. reserv.

01631504 SUPPLIER NUMBER: 18628120 (USE FORMAT 7 OR 9 FOR FULL TEXT)  
Clinical evidence of angiogenesis after arterial gene transfer of phVEGF165 in patient with ischaemic limb. (plasmid human vascular endothelial growth factor) (Early Reports)  
Isner, Jeffrey M.; Pieczek, Ann; Schainfeld, Robert; Blair, Richard; Haley, Laura; Asahara, Takayuki; Rosenfield, Kenneth; Razvi, Syed; Walsh, Kenneth; Symes, James F.  
The Lancet, v348, n9024, p370(5)  
August 10, 1996  
PUBLICATION FORMAT: Magazine/Journal ISSN: 0099-5355 LANGUAGE: English  
RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Professional  
WORD COUNT: 3057 LINE COUNT: 00257

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Display 5/3/13 (Item 4 from file: 149)

DIALOG(R) File 149:IAC(SM) Health&Wellness DB(SM)  
(c) 1997 Info Access Co. All rts. reserv.

01532789 SUPPLIER NUMBER: 17246660 (USE FORMAT 7 OR 9 FOR FULL TEXT)  
Curing disease through human gene therapy. (Pamphlet)  
Pamphlet by: National Heart, Lung, and Blood Institute, p1(38)  
July, 1993  
DOCUMENT TYPE: Pamphlet PUBLICATION FORMAT: Pamphlet LANGUAGE: English  
RECORD TYPE: Fulltext TARGET AUDIENCE: Consumer  
WORD COUNT: 7722 LINE COUNT: 00616

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Display 5/3/14 (Item 5 from file: 149)  
DIALOG(R) File 149:IAC(SM) Health&Wellness DB(SM)  
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01489566 SUPPLIER NUMBER: 15795484 (USE FORMAT 7 OR 9 FOR FULL TEXT)  
Expert: next two years critical for antiviral gene therapies. (Flossie  
Wong-Staal, X International Conference on AIDS)  
DeNoon, Daniel J.  
AIDS Weekly, p2(5)  
August 29, 1994  
PUBLICATION FORMAT: Newsletter ISSN: 1069-1456 LANGUAGE: English  
RECORD TYPE: Fulltext TARGET AUDIENCE: Professional  
WORD COUNT: 2422 LINE COUNT: 00235

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Display 5/3/15 (Item 6 from file: 149)  
DIALOG(R) File 149:IAC(SM) Health&Wellness DB(SM)  
(c) 1997 Info Access Co. All rts. reserv.

01481560 SUPPLIER NUMBER: 15414110 (USE FORMAT 7 OR 9 FOR FULL TEXT)  
Genes, dreams, and cancer. (gene therapy for cancer) (Current Issues in  
Cancer, part 8)  
Sikora, Karol  
British Medical Journal, v308, n6938, p1217(5)  
May 7, 1994  
PUBLICATION FORMAT: Magazine/Journal ISSN: 0959-8146 LANGUAGE: English  
RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Professional  
WORD COUNT: 2588 LINE COUNT: 00306

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Display 5/3/16 (Item 7 from file: 149)  
DIALOG(R) File 149:IAC(SM) Health&Wellness DB(SM)  
(c) 1997 Info Access Co. All rts. reserv.

01476996 SUPPLIER NUMBER: 14975260 (USE FORMAT 7 OR 9 FOR FULL TEXT)  
Cellular engineering and gene therapy strategies for insulin replacement in  
diabetes.  
Newgard, Christopher B.  
Diabetes, v43, n3, p341(10)  
March, 1994  
PUBLICATION FORMAT: Magazine/Journal ISSN: 0012-1797 LANGUAGE: English  
RECORD TYPE: Fulltext TARGET AUDIENCE: Professional  
WORD COUNT: 7818 LINE COUNT: 00803

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Display 5/3/17 (Item 8 from file: 149)  
DIALOG(R) File 149: Health&Wellness DB(SM)  
(c) 1997 Info Access Co. All rts. reserv.

01438071 SUPPLIER NUMBER: 14754403 (USE FORMAT 7 OR 9 FOR FULL TEXT)  
Progress toward human gene therapy.  
Morsy, Manal A.; Mitani, Kohnosuke; Clemens, Paula; Caskey, C. Thomas  
JAMA, The Journal of the American Medical Association, v270, n19, p2338(8)  
Nov 17, 1993  
PUBLICATION FORMAT: Magazine/Journal ISSN: 0098-7484 LANGUAGE: English  
RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Professional  
WORD COUNT: 9037 LINE COUNT: 00777

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Display 5/3/18 (Item 9 from file: 149)  
DIALOG(R) File 149:IAC(SM) Health&Wellness DB(SM)  
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01421140 SUPPLIER NUMBER: 14003767 (USE FORMAT 7 OR 9 FOR FULL TEXT)  
Molecular targets of gene transfer therapy for HIV infection.  
Buchsacher, Gary L., Jr.  
JAMA, The Journal of the American Medical Association, v269, n22, p2880(7)  
June 9, 1993  
PUBLICATION FORMAT: Magazine/Journal ISSN: 0098-7484 LANGUAGE: English  
RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Professional  
WORD COUNT: 7338 LINE COUNT: 00611

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Display 5/3/19 (Item 10 from file: 149)  
DIALOG(R) File 149:IAC(SM) Health&Wellness DB(SM)  
(c) 1997 Info Access Co. All rts. reserv.

01412277 SUPPLIER NUMBER: 13427568 (USE FORMAT 7 OR 9 FOR FULL TEXT)  
The pace of human gene transfer research quickens. (From the National  
Institutes of Health)  
Healy, Bernadine  
JAMA, The Journal of the American Medical Association, v269, n5, p567(1)  
Feb 3, 1993  
PUBLICATION FORMAT: Magazine/Journal ISSN: 0098-7484 LANGUAGE: English  
RECORD TYPE: Fulltext TARGET AUDIENCE: Professional  
WORD COUNT: 982 LINE COUNT: 00081

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Display 5/3/20 (Item 11 from file: 149)  
DIALOG(R) File 149:IAC(SM) Health&Wellness DB(SM)  
(c) 1997 Info Access Co. All rts. reserv.

01376664 SUPPLIER NUMBER: 14018048 (USE FORMAT 7 OR 9 FOR FULL TEXT)  
Gene transfer and gene therapy. (research and treatment applications)  
Nielsen, David A.; Goldman, David  
Alcohol Health & Research World, v16, n4, p304(8)  
Fall, 1992  
PUBLICATION FORMAT: Magazine/Journal ISSN: 0090-838X LANGUAGE: English  
RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Academic; Professional  
WORD COUNT: 5709 LINE COUNT: 00486

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Display 5/3/21 (Item 12 from file: 149)  
DIALOG(R) File 149: Health&Wellness DB(SM)  
(c) 1997 Info Access Co. All rts. reserv.

01357490 SUPPLIER NUMBER: 12182780 (USE FORMAT 7 OR 9 FOR FULL TEXT)  
Cystic fibrosis: molecular biology and therapeutic implications. (Biotech  
Special Report: Molecular Advances)  
Collins, Francis S.  
Science, v256, n5058, p774(6)  
May 8, 1992  
PUBLICATION FORMAT: Magazine/Journal ISSN: 0036-8075 LANGUAGE: English  
RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Academic  
WORD COUNT: 6227 LINE COUNT: 00504

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Display 5/3/22 (Item 13 from file: 149)  
DIALOG(R) File 149:IAC(SM) Health&Wellness DB(SM)  
(c) 1997 Info Access Co. All rts. reserv.

01355683 SUPPLIER NUMBER: 12141705 (USE FORMAT 7 OR 9 FOR FULL TEXT)  
Gene therapy for cancer. (review article)(includes glossary)  
Gutierrez, Andres A.; Lemoine, Nick R.; Sikora, Karol  
The Lancet, v339, n8795, p715(7)  
March 21, 1992  
PUBLICATION FORMAT: Magazine/Journal ISSN: 0099-5355 LANGUAGE: English  
RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Professional  
WORD COUNT: 4021 LINE COUNT: 00446

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Display 5/3/23 (Item 14 from file: 149)  
DIALOG(R) File 149:IAC(SM) Health&Wellness DB(SM)  
(c) 1997 Info Access Co. All rts. reserv.

01249601 SUPPLIER NUMBER: 09213094 (USE FORMAT 7 OR 9 FOR FULL TEXT)  
Cystic fibrosis: towards the ultimate therapy, slowly. (editorial)  
The Lancet, v336, n8725, p1224(2)  
Nov 17, 1990  
DOCUMENT TYPE: editorial PUBLICATION FORMAT: Magazine/Journal ISSN:  
0099-5355 LANGUAGE: English RECORD TYPE: Fulltext; Abstract  
TARGET AUDIENCE: Professional  
WORD COUNT: 691 LINE COUNT: 00075

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